REMARKS

The Examiner has indicated that the claims of US10/527,472 lack unity because the invention is not novel in view of the disclosure of US20060068472. Applicants respectfully disagree.

US20060068472 relates to compositions to ameliorate protein misfolding and aggregation. In paragraph [0233] cited by the Examiner, the potential origin of Parkinson's Disease and potential strategies are discussed. More particularly, with regard to caspase, it is stated in this section: "Overexpression of heat shock proteins can reduce the toxicity of both polyglutamine and mutant alpha-synuclein and caspase inhibition can reduce the toxicity of both polyglutamine and mutant SOD, indicating that therapeutic interventions of this type may apply across multiple neurodegenerative diseases." (emphasis added.)

Thus, this statement in US20060068472 teaches that caspase inhibition may have therapeutic benefit and may constitute an interesting therapeutic intervention. US20060068472 does not suggest providing a host organism lacking a functional caspase gene.

With regard to pharmaceutical screens, US20060068472 states: "Pharmaceutical screens are now underway to identify agents that block the expression or alter the processing and aggregation of the toxic proteins responsible for neurodegenerative disease, or mitigate the harmful effects of these proteins on neuronal function and

survival." Although caspase is identified in the statement recited above as an agent that can "reduce the toxicity of both polyglutamine and mutant SOD," there is no disclosure in US20060068472 that this agent itself is to be used in the further identification of other agents with similar activity, let alone that this agent would be used in the generation of an engineered yeast cell for screening of further agents with similar activity. More particularly, in view of the envisaged beneficial effects of caspase, US20060068472 does not disclose or suggest the generation of a host cell lacking a functional caspase gene.

In contrast with the disclosure of US20060068472, it was surprisingly found by the inventors of the present application that inhibition of expression of a caspase gene in yeast causes the toxic effects of amyloidogenic proteins to be more pronounced. In view of the alleged therapeutic properties attributed to caspase in the prior art including in US20060068472, the observation that caspase inhibition actually increased the toxic effect of amyloidogenic proteins in yeast was unexpected. However, it has allowed the inventors to generate a model system in yeast which, as a result of the lack of a functional caspase gene, allows an easier phenotypic reading of the heterologously expressed amyloidogenic protein. This is advantageous both for the analysis of the mechanism of neurodegenerative diseases and for the screening of potential therapeutic agents or drug targets for use in the treatment of amyloidogenic neuropathies, as the effects of potential therapeutic agents can be more easily observed in this model system.

Based on the above it is submitted that the restriction requirement is inappropriate,

and applicants respectfully request that all of the claims be examined together.

CONCLUSION

If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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